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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,413	11/21/2001	Nancy Allbritton	Q048	6314

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EXAMINER	
LY, CHEYNE D	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,413	ALLBRITTON ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-101* is/are pending in the application.

4a) Of the above claim(s) *83-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-82 and 86-101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *66-101* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/19/04*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *7/21/03* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' arguments filed March 19, 2004 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. The cancellation of claims 1-65 and addition of claims 66-101 have been acknowledged.

3. The species election requirement directed to elected claims 10-22 and 24-45 for Species A, C, D, E, and F, has been withdrawn because claims 1-65 have been cancelled.

4. The species election requirement directed to Species (B) has been maintained due to said species being recited in claims 82-85.

5. Newly submitted claims 83-85 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 83-85 are directed to the non-elected species recited in the original claim 39; therefore, said claims have been withdrawn from prosecution.

6. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 83-85 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

7. Claims 66-82 and 86-101, Species (B), two-dimensional gel electrophoresis, are examined on the merits.

PRIORITY

8. Applicant's argument of the provisional application 60/252,861 provides priority benefit support to the limitation of "detecting activity" has been found to be unpersuasive because the pointed to disclosure in said provisional application discloses "a method of detecting protein activity in a cell" which is completely different from the claimed invention of "detecting activities of a plurality of different proteins in a cell". It is noted that the disclosure of a method for detecting a protein activity in a cell does not provide priority benefit support for the claimed invention of "detecting activities of a plurality of different proteins in a cell".

9. Specific to the limitation of "microinjection", Applicant's argument is considered to be moot due to the cancellation of claims 1-65.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 66-82 and 86-101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. This rejection is necessitated by Applicants amendments.

13. Specific to claim 66, the preamble recites "A method for detecting the activities of a plurality of different proteins in a cell" while the steps of said claim detect "reporter molecules" which causes said claim to be vague and indefinite. Claim 66 is unclear as to whether the claimed invention is directed to detecting the activities of a plurality of different

proteins in a cell or detecting "reporter molecules". The limitation of "reporter molecules" could reasonably be construed as a plurality of homogenous molecules. Therefore, claim 66 is unclear as to which step if any detects the activities of a plurality of different proteins in a cell. Does the preamble or the body of the claim control the metes and bounds of the claim? Clarification of the metes and bounds of the instant claim is required. Claims 67-82 and 86-101 are rejected for being dependent from claim 66.

14. Specific to claim 101, Applicant uses the abbreviations of "pl". Abbreviations in claims are vague and indefinite unless accompanied by the full name, usually in parentheses.

CLAIM REJECTIONS - 35 USC § 112

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 66-82 and 86-101 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. NEW MATTER REJECTION.

17. This rejection is necessitated by Applicants amendments.

18. Specific to claim 66, lines 1 and 5-6, the limitation of "activities of ...of different proteins in a cell" has not been found in the original claims 10-45 or the instant specification. It is noted that the instant specification discloses the limitations of a plurality of proteins in a cell (page 10, lines 1-12), and a database comprising the activities of different proteins (page

17, line 20); however, the above disclosures do not support the limitation of "activities of ...of different proteins in a cell". The disclosure of a plurality of proteins in a cell could reasonably be construed as a plurality of homogenous molecules. Claims 67-82 and 86-101are rejected for being dependent from claim 66.

19. Specific to claim 71, line 2, the limitation of "small molecule" has not been found in the original claims 10-45 or the instant specification. It is noted that the limitation of "compound" is disclosed throughout the instant specification. However, the limited disclosure of "compound" does not provided written basis support for the broader limitation of "small molecule" as recited in claim 71.

20. Specific to claim 71, which depends from claims 70 and 69, the limitation of a stimulus compound that is "a nucleic acid" has not been found in the original claims 10-45 or the instant specification. It is noted that the instant specification discloses DNA arrays (page 10, line 4). However, the disclosure of DNA arrays is completely different from the limitation of "a nucleic acid" being used as a stimulus compound.

21. Specific to claims 86-90, line 1, which depend from claim 66, the limitation of "different proteins" has not been found in the original claims 10-45 or the instant specification. It is noted that the instant specification discloses the limitations of a plurality of proteins in a cell (page 10, lines 1-12), and a database comprising the activities of different proteins (page 17, line 20); however, the above disclosures do not support the limitation of "activities of ...of different proteins in a cell". The disclosure of a plurality of proteins in a cell could reasonably be construed as a plurality of homogenous molecules.

22. Specific to claims 92-94, line 2, the limitations of "at most" 1 micromolar, 10 micromolar, or 100 nanomolar has not been found in the original claims 10-45 or the instant specification. It is noted that the original claims 24-26 disclose the limitations of "less than or equal to" 1 micromolar, 10 micromolar, or 100 nanomolar which is completely different from the limitations of claims 92-94, respectively.

23. Specific to claims 99 and 100, lines 1-2, the limitation of quantifying the activities of at least three, or ten proteins has not been found in the original claims 10-45 or the instant specification. It is noted that claims 5 and 9 of the original claims recited detecting a single protein activity of three/ten or more proteins. The recitation of the limitation of detecting a single activity is completely different from the limitation of detecting a plurality of activities as recited in new claims 99 and 100.

24. Specific to claim 101, the limitation of "the cell has a volume of 100 pl or less" has not been found in the original claims 10-45 or the instant specification.

CLAIM REJECTIONS - 35 USC § 103

25. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

26. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent

any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

27. Claims 66-82 and 86-101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Day et al. (1998) taken with Sims et al. (1998) in view of Wright (US 5,639,656 A).

28. This rejection is necessitated by Applicants amendments.

RESPONSE TO ARGUMENT

29. Applicant's argument of the combination of Day et al., Sims et al., and Wright does not disclose the limitation of "detecting the activities of a plurality of different proteins with reporter molecules" has been fully considered and found to be unpersuasive as discussed below.

30. Day et al. discloses a method of detecting protein activity in a cell comprising introducing the reporter molecules luciferase (Luc) and green fluorescent protein (GF) via a vector (Figure 1) into GH3 and Hela cells (activities of different proteins) (page 848, column 3, lines 32-42 and page 850, column 1, lines 1-30). The reporter molecules are released for electrophoresis (page 850, column 1, lines 33-56). The reporter molecules are identified by fluorescence microscopy (Figure 2) and electrophoresis by first boiling reporter molecule to terminate chemical reaction and by dilution of anti-GFP antibody to diminish chemical reaction (page 850, column 1, lines 33-56), as in instant claims 66 and 101. Due to the vague and indefinite issue of claim 101, the disclosure of Day et al. above is consistent with the limitations of claim 101.

31. The reporter molecules are detected as GFP (unaltered) or GFP-Luc (altered) (Figure 1), as in instant claim 67.

32. Figure 2 discloses activities of GFP and Luc proteins as recorded and in a tabulated form. The limitation of "tabulating" has been construed as to form with a plane surface, as in instant claim 68.

33. The cells were exposed to hygromycin and luciferin external stimuli prior to releasing the reporter molecules (page 582, lines 7-28), as in instant claims 69-71.

34. Figures 2a and b, and Figures 3a, b, and c, provide a map of cellular responses to a compound, as in instant claim 72.

35. The transfection of GH3 cells (enter) is performed with GFP attached to Luc protein via a vector (page 852, column 1, lines 7-11), as in instant claims 73 and 74.

36. Western blots are used with GFP-specific antibody (first label) and Luc-specific antibody (second label) and fluorescence microscopy is used to detect expression (Figure 3), as in instant claims 75-77.

37. Fusion of protein motif from cyclin that contributes to rapid protein degradation (releasing) which result in a destabilized protein. The treatment of GH3 cells with translation-inhibitor Chx is used to estimate the turnover (releasing) of Luc and GFP activity and the inactivation of Luc (stop) (pages 852-853, Recombinant Reporter Stability). The chemical reaction is also terminated by adding cycloheximide (page 852, column 1, lines 23-30), as in instant claims 78 and 95-98.

38. The method of Day et al. detects the activity of GFP, Luc, Luc-GFP fusion protein, anti-Luc antibody, anti-GFP antibody, an anti-rabbit Ig, and horseradish peroxidase (six proteins)

(page 850, Immunoprecipitation and Western Blotting §, and Figures 1 and 2), as in instant claims 86-89 and 99. Due to the vague and indefinite issue of claim 66 from which claims 86-89 and 99 depend, the disclosure of Day et al. above is consistent with the limitations of claims 86-89 and 99.

39. However, Day et al. does not disclose the use of 2-D electrophoresis for the method of detecting protein activity portion of a cell.

40. Wright et al. discloses a method of identifying report molecules from cells by 2-D electrophoresis (column 16, line 64 to column 17, line 6), as in instant claim 82.

41. Sims et al. discloses a method of detecting protein activity in a cell, portion of a cell or group of cells by microinjecting labeled IP3 at concentration of 100 nM into oocytes (Abstract etc.). The results are compiled in a tabulation of protein activity as directed to the reporter molecule, IP3, (page 4057, Table I), as in instant claims 91-94.

42. The method of Sims et al. suggests the detection and quantification of at least 10 proteins for their activity; starting with several forms of 5-phosphatase to centrauin-α and proteins involved in IP3 degradative pathways (page 4052, column 2, lines 1-25), as in instant claims 90 and 100.

43. At various time points (0-300 seconds) the reactions are stopped, inositol phosphates are isolated and separated by HPLC (Figure 2 B), as in instant claims 79-81.

44. Day et al. suggests an improvement via recent advances in digital imaging systems for visualizing events as they occur with the living cell by detecting protein activity with reporter molecules (page 848, column 2, lines 1-6). The improvement suggested by Day et al. comprises detecting and releasing reporter molecules by protein isolation (pages 848-853,

Materials and Methods §). Wright et al. discloses a method of identifying report molecules from cells by 2-D electrophoresis (column 16, line 64 to column 17, line 6). Sims et al. discloses method of detecting protein activity in a cell, portion of a cell or group of cells by microinjecting labeled IP3 (Abstract etc.). Thus, the improvement suggested by Day et al. is directly applicable to the methods of isolating reporter molecules for the detection of protein activity as taught by Sims et al., and Wright et al.

45. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement suggested by Day et al. to use a method of detecting protein activity in a cell comprising introducing the reporter molecules wherein said method requires 2-D gel electrophoresis. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use a method of detecting protein activity in a cell, portion of a cell or group of cells comprising introducing the reporter molecules wherein said method requires the limitation of 2-D gel electrophoresis as taught by Day et al., Sims et al., and Wright et al.

CONCLUSION

46. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

47. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory

period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

48. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

49. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

50. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

51. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

C. Dune Ly
5/27/04

John D Marshall 5/28/04
JOHN H. MARSCHEL